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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/718,989	11/21/2003	Xuedong Song	KCX-741 (19044)	9109

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EXAMINER	
DIRAMIO, JACQUELINE A	
ART UNIT	**PAPER NUMBER**
1641	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)
	10/718,989	SONG, XUEDONG
	Examiner	Art Unit
	Jacqueline DiRamio	1641

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on 27 February 2006.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 64-88 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 64-88 is/are rejected.

7)☒ Claim(s) 77 is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on 15 April 2004 is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the Claims

The cancellation of claims 1-63 is acknowledged. Currently, new claims 64 – 88 are pending.

Withdrawn Objections and Rejections

All objections and rejections of claims 1 – 43 in the previous office action have been withdrawn in light of the cancellation of these claims in the amendment filed February 27, 2006.

Response to Arguments

Applicant's arguments, p7-8, with respect to the Rylatt et al. reference (WO 97/009620) and the Klimant reference (US 6,770,220) have been considered and are persuasive with regards to the references not providing distinct motivation for combining phosphorescent particles with a "lateral flow, membrane-based device." Additionally, the added limitation in new claim 64 of the phosphorescent label having an emission lifetime of about 1 microsecond or more is not taught by either of these references, and therefore the combined references cannot be obvious over this limitation. Therefore, the newly added claims 64 – 88 are not obvious over Rylatt et al. in view of Klimant, but the claims are unpatentable over Daniels et al. (US 2002/0004246) in view of O'Riordan et al. ("Performance Evaluation of the Phosphorescent Porphyin Label: Solid-Phase Immunoassay of α-Fetoprotein," *Anal. Chem.* 74 (2002) 5845-5850), and further in view of Klimant (US 6,770,220) as discussed below in the NEW GROUNDS FOR REJECTION.

NEW GROUNDS OF REJECTION

Claim Objections

Claim 77 is objected to because of the following informalities:

Claim 77 recites the phrase “has an emission lifetime of **from** about 100 to about 1000 microseconds,” which appears to be incorrect because of the extra word “from” which is not included in the similar recitation found in claim 76.

Appropriate correction is required.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 64 – 84 are rejected under 35 U.S.C. 103(a) as being unpatentable over Daniels et al. (US 2002/0004246) in view of O’Riordan et al. (“Performance Evaluation

of the Phosphorescent Porphyin Label: Solid-Phase Immunoassay of α-Fetoprotein," *Anal. Chem.* 74 (2002) 5845-5850), and further in view of Klimant (US 6,770,220).

Daniels et al. teach a method for detecting an analyte within a test sample, the method comprising:

i) providing a lateral flow test strip (assay device) that comprises a porous membrane in fluid communication with semiconductor nanocrystals (luminescent or phosphorescent particles) conjugated with a specific binding member, wherein the porous membrane defines a capture region (detection zone) within which is immobilized a capture reagent;

ii) contacting the lateral flow test strip with the test sample;

iii) subjecting the capture region to light at a selected excitation wavelength (one pulse of illumination) to generate a detection signal; and

iv) thereafter, measuring the intensity of the detection signal, wherein the amount of the analyte within the test sample is proportional to the intensity of the detection signal (see Figure 1; and paragraphs [0016]-[0028], [0079]-[0082], [0095], [0109], [0111], [0115]-[0120], [0126]-[0128], [0170], and [0212]-[0215]).

However, Daniels et al. fail to teach that the luminescent/phosphorescent particle has an emission lifetime of about 1 microsecond or more or that the particles is a phosphorescent label encapsulated within a matrix.

O'Riordan et al. teach a solid-phase immunoassay utilizing phosphorescent porphyin labels, particularly platinum(II)-coproporphyrin-I, which display high quantum yields, long phosphorescent lifetimes in the 10-1000 microsecond range and intense

absorption bands, allowing for high sensitivity during assays (see p5845, paragraph 2). The measurement of the phosphorescent labels was accomplished by excitation with a 1 – 50-μs square pulse, a 50-μs delay time, 100-μs gate time, and a 1-s integration time, which gave the highest signal/noise ratio and therefore, used as the standard parameters for signal emission and detection (see p5848, *Evaluation of Instrument Performance*).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to combine with the detection method of Daniels et al. the phosphorescent porphyin labels, as well as the excitation and signal detection parameters taught by O'Riordan et al. wherein a pulsed excitation source (illumination) is utilized because O'Riordan et al. teach the benefit of these labels because of their high quantum yields, long phosphorescent lifetimes in the 10-1000 microsecond range and intense absorption bands, which allow for high sensitivity during assays, as well as the benefit of this type of phosphorescent excitation and signal detection because of its high signal/noise ratio.

However, O'Riordan et al. fail to include the limitation of encapsulating the phosphorescent label within a matrix.

Klimant teaches of the production and use of luminescent microparticles wherein phosphorescent labels are incorporated (encapsulated) within solid particles for use as internal standards for referencing phosphorescence signals or as markers for labeling and detecting biomolecules (see column 1, lines 1-9). Luminescence measurements using phosphorescence signals is a very common method in biological and chemical

analysis dues to its high sensitivity and versatility (see column 1, lines 30-35). The incorporation of the phosphorescence labels within matrices allows for elimination or great reduction in phosphorescence signal quenching by interfering oxygen that is common during luminescence measurement (see column 1, lines 17-23).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to combine with the detection method of Daniels et al. and the phosphorescent labels of O'Riordan et al. the encapsulation of the phosphorescent label within a matrix as taught by Klimant because Klimant teaches the benefit of incorporation of phosphorescence labels within matrices in order to eliminate or greatly reduce phosphorescence signal quenching by interfering oxygen that is common during luminescence measurement.

With respect to Applicant's claims 65, 66, and 68, Klimant teaches that the phosphorescent label is a metal/ligand complex, particularly comprised of transition metals such as ruthenium, osmium, iridium, rhenium, platinum, or palladium, and also containing complex ligands, such as **bipyridine**, bipyrazine, phenanthroline, terpyridil or derivatives thereof (see column 3, lines 14-21).

With respect to Applicant's claims 67 and 69, Klimant teaches the phosphorescent label can further comprise a porphyrin ligand or porphyrin complex with platinum(II) or palladium(II), which anticipates Applicant's claims 7 and 31 because the porphyin complexes encompass the derivatives and combinations thereof and are being utilized for the same purpose (see column 3, lines 25-31).

With respect to Applicant's claim 70, Klimant teaches the matrix incorporating the phosphorescent label comprises polymer particles (see column 4, lines 11-19).

With respect to Applicant's claims 71 and 72, Klimant teaches the size of the luminescent particles in the range of 20 µm to 10 µm, particularly from 50 nm to 1 µm (see column 3, lines 37-39).

With respect to Applicant's claim 73, Klimant teaches the matrix incorporating the phosphorescent label protects the label from quenching (see column 1, lines 17-23).

With respect to Applicant's claims 74 and 75, Klimant teaches the matrix incorporating the phosphorescent label protects the label from quenching, enabling the luminescence lifetime (detection signal) to be only 20%, at most 15% and preferably at most 10% shorter than in an O_2 free environment, which anticipates Applicant's claims 74 and 75 (see column 3, lines 5-13).

With respect to Applicant's claims 76 and 77, O'Riordan et al. teach the phosphorescent labels have an emission lifetime of 10-1000 microseconds (see p5845, second column).

With respect to Applicant's claim 78, O'Riordan et al. teach that the detection signal is measured with a 50-microsecond delay time and utilizes a pulsed illumination (see p5848, under "Evaluation of Instrument Performance").

With respect to Applicant's claim 79, Daniels et al. teach that the capture reagent in the capture region comprises a specific binding member, such as an antigen, hapten, antibody, or streptavidin (see Figures 1 and 2; and paragraphs [0025], [0088]-[0090], and [0116]).

With respect to Applicant's claims 80 and 81, O'Riordan et al. teach that the illumination is provided by a pulsed excitation source and the detection signal is measured by a time-gated detector (see see p5848, under "Evaluation of Instrument Performance").

With respect to Applicant's claims 82-84, Daniels et al. teach that the specific binding member that is conjugated to the luminescent particles, i.e. semiconductor nanocrystals, is configured to preferentially bind with the analyte and can comprise antigens, haptens, aptamers, and antibodies, as well as analogs of the analyte itself (see paragraphs [0016], [0024], [0088]-[0090], and [0094]-[0098]).

Claims 85 and 86 are rejected under 35 U.S.C. 103(a) as being unpatentable over Daniels et al. (US 2002/0004246) in view of O'Riordan et al. ("Performance Evaluation of the Phosphorescent Porphyin Label: Solid-Phase Immunoassay of α-Fetoprotein," *Anal. Chem.* 74 (2002) 5845-5850), and Klimant (US 6,770,220), as applied to claim 64 above, and further in view of Rylatt et al. (WO 97/009620).

Daniels et al. teach an additional control line or region, but fail to teach that the control line works as a calibration zone, wherein the intensity of the detection signal is calibrated by the intensity of the calibration signal. Neither O'Riordan et al. of Klimant teach the use of a calibration zone.

Rylatt et al. teach a method for quantitative determination of a target analyte in a test sample, comprising a lateral flow assay device wherein a liquid permeable membrane (porous membrane) is used, wherein said membrane contains a test zone

(detection zone) and at least one calibration zone(s) (see p4, lines 29-30 and p5, lines 1-20). The membrane also utilizes an analyte detection agent (detection probe) comprising a specific binding partner and an associated label (see p7, lines 25-29 in particular). The test zone (detection zone) utilizes an immobilized analyte receptor (capture reagent) that can bind with the analyte and/or analyte detection agent (detection probe) and generate a detectable signal. The calibration zone includes an immobilized calibration agent receptor that binds to the specific binding partner found on the analyte detection agent (detection probe) or calibration agent (calibration probe) and further, the binding of the agent to the calibration zone produces a calibration signal that is used to calibrate the signal produced in the test zone (detection signal) (see p5, lines 10-20 and p9, lines 13-19 in particular). Therefore, the lateral flow membrane, containing the analyte detection agent (detection probes), is contacted with the test sample; the analyte detection agent (detection probes) binds to the target analyte and flows to the test zone (detection zone) wherein it binds to an immobilized analyte receptor, and generates a signal, which is detected and measured, thus providing the amount of analyte in the test sample, which is proportional to the intensity of the signal at the test zone (detection signal) calibrated by the intensity of the calibration signal (see p18-20 in particular).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to include with the detection method of Daniels et al., O'Riordan et al., and Klimant a calibration zone as taught by Rylatt et al. because Rylatt et al. teach the benefit of including a calibration zone with a test zone on a lateral flow

assay device in order to provide accurate quantitative determination of a target analyte in a test sample, because the signal produced in the calibration zone is utilized to calibrate the signal produced in the test zone.

Claims 87 and 88 are rejected under 35 U.S.C. 103(a) as being unpatentable over Daniels et al. (US 2002/0004246) in view of O'Riordan et al. ("Performance Evaluation of the Phosphorescent Porphyin Label: Solid-Phase Immunoassay of α-Fetoprotein," *Anal. Chem.* 74 (2002) 5845-5850), and Klimant (US 6,770,220), as applied to claim 64 above, and further in view of Zarling et al. (US 5,674,698).

The Daniels et al., O'Riordan et al., and Klimant references fail to teach that the phosphorescent labels/particles have a Stokes shift of about 50 to 100 nanometers or more.

Zarling et al. teach of up-converting and down-converting phosphorescent/luminescent reporters for use in biological assays using laser excitation techniques. Down-converting luminescent labels, which comprise inorganic phosphors, are discussed with respect to their Stokes shift, which is typically at least 100 nanometers. The large Stokes shift of a phosphor label is beneficial because it aids in the discrimination of signal from scattered excitation light. Further, the phosphors possess sufficiently long emission lifetimes, i.e. greater than 1 microsecond, permitting their use in time-gated detection methods, which can reduce noise caused by shorter-lived autofluorescence and scattered excitation light (see column 1, lines 12-18; and column 4, lines 8-31).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to include with the detection method of Daniels et al., O'Riordan et al., and Klimant the use of phosphorescent labels with large Stokes shifts, at least 50 to 100 nanometers or more, as taught by Zarling et al. because Zarling et al. teach that a phosphor label with a large Stokes shift is beneficial because it aids in the discrimination of signal from scattered excitation light, and further the use of this type of phosphorescent label that also includes a sufficiently long emission lifetime, i.e. greater than 1 microsecond, and is utilized with time-gated detection methods can reduce noise caused by shorter-lived autofluorescence and scattered excitation light.

Conclusion

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jacqueline DiRamio whose telephone number is 571-272-8785. The examiner can normally be reached on M-F 9-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on 571-272-0823. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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